IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: KEARNEY *et al.*

Serial No.:   10/719,916

Filed: November 21, 2003

Examiner: LIN, Jerry

Group Art Unit: 1631

Title: CONSTELLATION MAPPING AND USES THEREOF

Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

DECLARATION OF PAUL KEARNEY UNDER 37 C.F.R. § 1.132

I, Paul E. KEARNEY, Ph.D., being duly warned that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent resulting therefrom, declare that:

1. I am an inventor of the subject matter described and claimed in the above-captioned patent application.

2. From January 1, 2001 until February 1, 2008 I was continuously employed by Caprion Proteomics Inc. (Caprion) and its predecessors in business. Prior to an amalgamation in 2007, Caprion was known as Caprion Pharmaceuticals Inc., which is the assignee of record for the above-captioned patent application. Prior to the end of my employment by Caprion, I was Caprion's Vice-President of Bioinformatics. During the time in which I was employed at Caprion, my duties included the management of the bioinformatics and IT departments, coordinating data analysis, managing the development of scientific software, coordinating proteomic research and development and participating in business development activities.

3.   I have read the application and the Office Action mailed on October 31, 2007.

4.   At page 29, lines 8-15 of the application, retention time clustering is described. Retention time clustering involves "sorting the peptides in p from low to high retention time" where p refers to peptide p in peptide map A, which is being matched to peptides in peptide map B. Sorting is a standard algorithm available even in commercial software such as Microsoft Excel. It is also one of the first algorithmic procedures taught to undergraduate students in computer science courses. For example, sorting is taught in the undergraduate textbook *Introduction to Algorithms* by Cormen, Leiserson and Rivest, The MIT Press 1990 (see Section II (Sorting and Order Statistics)) attached hereto as Exhibit A.

5.   As stated at page 29, lines 11-12 of the application, retention time clustering also involves "grouping peptides into clusters of peptides of similar retention time (i.e. within a predefined difference)" and such groupings are called "retention time clusters". The grouping of peptides by similar retention time can be achieved by those in the computer science field using any one of a number of standard procedures such as hierarchical clustering, k-means clustering, multidimensional scaling or simple histogram analysis. Grouping of peptides along the retention time dimension is an instance of a generic problem of clustering objects along some dimension (in this instance it is retention time). Clustering is a well-known procedure in the computer science field; numerous articles, tutorials and text books have been written on the subject including an article by A. K. Jain, M. N. Murty and P. J. Flynn entitled *Data Clustering: A Review* (ACM Computing Surveys, Vol. 31, No.3, p.264-323, 1999) a copy of which is attached hereto as Exhibit B; and a textbook by R. O. Duda and P. E. Hart: *Pattern Classification and Scene Analysis*, Wiley and Sons, 1973 (see Chapter 6 (Unsupervised Learning and Clustering)), a copy of which is attached hereto as Exhibit C.

6.   The column offset is determined by performing the steps described above in paragraphs 4 and 5 (i.e., sorting the peptides and grouping the peptides into retention time clusters). Once these two steps are performed, the column offset can be

determined. As stated at page, 29, lines 14-15 of the application, "the distribution mode is used to determine the column offset but any measure of centrality can be used." The mode of a distribution, and more generally, measures of centrality such as median and mean, are well-defined concepts found in any introductory statistics textbook and are easily applied by someone working in the area of computer science. One example of a textbook that teaches modes of distribution and measures of centrality is J. H. Zar, *Biostatistical Analysis*, Prentice Hall, 1999 (see Chapter 3 (Measures of Central Tendency)), a copy of which is attached hereto as Exhibit D.

7.   As stated at page 29, lines 21-22, "Algorithmically, the optimum retention time adjustment can be determined by many approaches including integer programming." Integer programming is a standard algorithmic concept known to those practicing in the area of computer science. Integer programming is taught in many standard textbooks, including, for example, H. M. Salkin, *Integer Programming*, Addison-Wesley, 1975 (see Chapter 1 (Introduction to Integer Programming)), a copy of which is attached hereto as Exhibit E.

8.   As stated at page 29, lines 24-25 of the application, "[a] median smoothing window is applied along retention time to obtain local retention time offset values. This results in the blue line depicted in FIG. 17." Median smoothing window is a concept taught in introductory signal processing and statistics courses. Median smoothing is defined in, for example, L. Fahrmeir and G. Tutz, *Multivariate Statistical Modeling Based on Generalized Linear Models,* Springer-Verlag, 1994 (see Section 5.1.1. (Simple neighborhood smoothers)), a copy of which is attached hereto as Exhibit F.

9.   All statements made herein of my own knowledge are true, and all statements made on information and belief are believed to be true.

Date: _Apr 29/08_

Paul Kearney